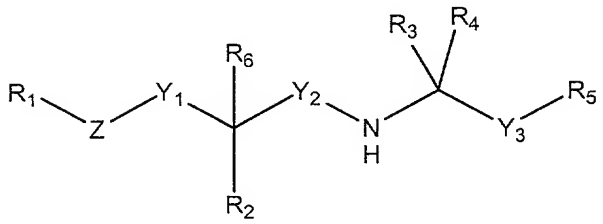
CLAIMS

1. A compound having the chemical formula:



wherein R_1 is selected from the group consisting of: heteroaryl and heterocycloalk;

R_2 is selected from the group consisting of: lower alk, cycloalk, alkoxy, H, OH, =O. C(O)OH, C(O)O-lower alk, C(O)NH-lower alk, C(O)N(lower alk)$_2$, SH, S-lower alk, NH_2, NH-lower alk, and N(lower alk)$_2$,

R_3 and R_4 is each independently lower alk or together cyclopropyl;

R_5 is either an optionally substituted naphthyl having one to four substituents independently selected from the group consisting of methyl, ethyl, isopropyl, methoxy, Cl, F, Br, and lower haloalkoxy, or a substituted phenyl having one to four substituents with at least one substituent in a *meta* or *para* position selected from the group consisting of: lower alkyl, methoxy, Cl, F, Br, and lower haloalkoxy, provided that said substituted phenyl may also have 2 to 3 additional substituents;

R_6 if present is either hydrogen, lower alkyl or lower alkenyl, wherein R_6 is not present if R_2 is =O;

Y_1 is either covalent bond, alkylene, or alkenylene;

Y_2 is alkylene;

Y_3 is alkylene;

Z is selected from the group consisting of: covalent bond, O, S, NH, N-lower alk, alkylene, alkenylene, and alkynylene, provided that if Z is either O, S, NH, or N-lower alk, then Y_1 is not a covalent bond; further provided that Y_1 and Z may together be a covalent bond;

further provided that if R_5 is 3, 4 dimethoxy-phenyl, then R_1 is not $CH_3(CH_2)_5O$-phenyl; 2-cyclopentyl, phenyl; 2-Cl-phenyl; 2-CN-phenyl; 2-(3-furanyl)phenyl; or 4-benzo(d)isothiazole;

further provided that if R_5 is 4-methoxy-phenyl, then R_1 is not 2-cyclopentyl-phenyl; 2-CH_3-phenyl; 2-benzyl-phenyl; 3-CH_3-phenyl, 4-CH_3SO_2-phenyl, 4-benzo(d)isothiazole;

further provided that if R_5 is 4-Cl-phenyl, then R_1 is not 2-CH_3-phenyl, 5-iso-propyl-phenyl; 4-CH_3-phenyl; phenyl; 2-Cl-phenyl; 4-Cl-phenyl; 2-methoxy, 4-CH_3CHCH-phenyl; 3,4 CH_3-phenyl, 2,4 CH_3-phenyl; 2,3 CH_3-phenyl; 2-iso-propyl, 5-CH_3-phenyl; pyridyl; 1-imidazole; or 4-benzo(d)isothiazole; and

further provided that if R_5 is 3,5 dimethyl, 4-methoxy-phenyl, then R_1 is not 4-CH_3, 6-CN-2-pyridyl; or thiophenecarboxamide; and

pharmaceutically acceptable salts and complexes thereof;

wherein said compound has an $IC_{50} \leq 10$ μM using the Calcium Receptor Inhibitor Assay.

2. The compound of claim 1, wherein

Y_1 is methylene;

Y_2 is methylene; and

Y_3 is methylene.

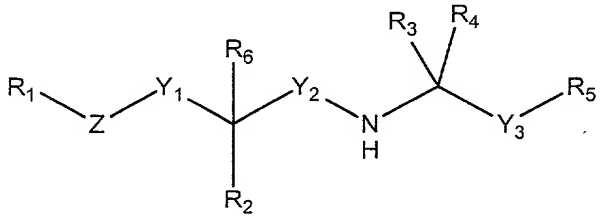
3. The compound of any of claims 1-2, wherein
R_2 is OH or methoxy,
R_6 is hydrogen,
R_3 or R_4 is independently methyl or ethyl; and
Z is O, S, or unsubstituted alkylene.

4. The compound of claim 3, wherein R_2 is OH, and Z is O.

5. The compound of claims 1-2, wherein
R_2 is hydrogen,
R_6 is hydrogen,
R_3 and R_4 is independently methyl or ethyl; and
Z is O or methylene.

6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the compound of claims 1-3.

7. A method of treating a patient comprising the step of administering to said patient a therapeutically effective amount of a compound having the formula:



wherein R_1 is selected from the group consisting of: heteroaryl and heterocycloalk;

R_2 is selected from the group consisting of: lower alk, cycloalk, alkoxy, H, OH, =O, C(O)OH, C(O)O-lower alk, C(O)NH-lower alk, $C(O)N(\text{lower alk})_2$, SH, S-lower alk, NH_2, NH-lower alk, and $N(\text{lower alk})_2$;

R_3 and R_4 is each independently lower alk or together cyclopropyl;

R_5 is aryl;

R_6 if present is either hydrogen, lower alkyl or lower alkenyl, wherein R_6 is not present if R_2 is =O;

Y_1 is either covalent bond, alkylene, or alkenylene;

Y_2 is alkylene;

Y_3 is alkylene;

Z is selected from the group consisting of: covalent bond, O, S, NH, N-lower alk, alkylene, alkenylene, and alkynylene, provided that if Z is either O, Z, NH, or N-lower alk, then Y_1 is not a covalent bond; further provided that Y_1 and Z may together be a covalent bond; and

pharmaceutically acceptable salts and complexes thereof;

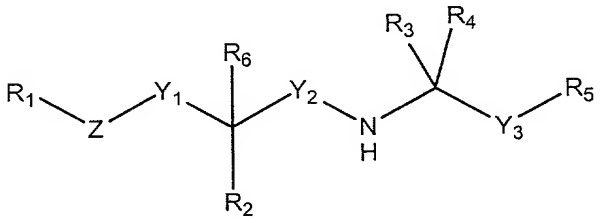
wherein said patient has a disease or disorder characterized by one or more of the following: (1) an abnormal bone or mineral homeostasis; (2) an abnormal amount of an extracellular or intracellular messenger which is ameliorated by a compound able to effect one or more calcium receptor activities; or (3) an abnormal effect of an intracellular or extracellular messenger which is ameliorated by a compound able to affect one or more calcium receptor activities.

8. The method of claim 7, wherein said disease or disorder is characterized by said abnormal bone or mineral homeostasis.

9. The method of claim 7, wherein said disease or disorder is selected from the group consisting of: osteosarcoma, periodontal disease, fracture healing, osteoarthritis, rheumatoid arthritis, Paget's disease, humoral hypercalcemia malignancy, and osteoporosis.

10. The method of claim 9, wherein disease or disorder is osteoporosis.

11. A method of treating a patient comprising the step of administering to said patient an amount of a compound sufficient to increase serum PTH level, said compound having the formula:



wherein R_1 is selected from the group consisting of: heteroaryl and heterocycloalk;

R_2 is selected from the group consisting of: lower alk, cycloalk, alkoxy, H, OH, =O, C(O)OH, C(O)O-lower alk, C(O)NH-lower alk, C(O)N(lower alk)$_2$, SH, S-lower alk, NH_2, NH-lower alk, and N(lower alk)$_2$;

R_3 and R_4 is each independently lower alk or together cyclopropyl;

R_5 is aryl;

R_6 if present is either hydrogen, lower alkyl or lower alkenyl, wherein R_6 is not present if R_2 is =O;

Y_1 is either covalent bond, alkylene, or alkenylene;

Y_2 is alkylene;

Y_3 is alkylene

Z is selected from the group consisting of: covalent bond, O, S, NH, N-lower alk, alkylene, alkenylene, and alkynylene, provided that if Z is either O, S, NH, or N-lower alk, then Y_1 is not a covalent bond; further provided that Y_1 and Z may together be a covalent bond; and

pharmaceutically acceptable salts and complexes thereof.

12. The method of claim 11, wherein said compound is administered to said patient causes an increase in serum PTH having a duration of one to twelve hours.

13. The method of claim 11, wherein said method is carried out by administering an amount of said compound effective causes an increase in either duration, quantity, or both duration and quantity, of serum PTH level sufficient to have a therapeutic effect.

14. The method of claim 13, wherein said compound is administered to said patient causes an increase in serum PTH having a duration of one to twelve hours.

15. The method of claim 14, wherein said duration is about two to about four hours.

16. The method of claim 13, wherein said compound is administered to said patient causes an increase in serum PTH up to 0.5 fold greater than peak serum PTH in said patient.

17. The method of claim 13, wherein said compound is administered to said patient causes an increase in serum PTH 0.5 fold to 5 fold greater than peak serum PTH in said patient.

18. The method of claim 13, wherein said compound is administered to said patient causes an increase in serum PTH 5 fold to 10 fold greater than peak serum PTH in said patient.

19. The method of claim 13, wherein said compound is administered to said patient causes an increase in serum PTH at least 10 fold greater than peak serum PTH in said patient.

20. The method of any of claims 7-19, wherein R_5 is a substituted phenyl having one to four substituents each independently selected from the group consisting of: methoxy, lower alkyl, OCF_3, CFH_2, CHF_2, CF_3, OHC_2CF_3, F, Cl, Br, I, OH, SH, CN, NO_2, NH_2, methylene dioxy, NH-lower alkyl, N(lower alkyl)$_2$, C(O)lower alkyl, SC(O)lower alkyl, $S(O)_2$ lower alkyl, OC(O)lower alkyl, SC(O)lower alkyl, OC(S)lower alkyl, NHC(O)lower alkyl, N(lower alkyl)C(O)lower alkyl, NHC(S) lower alkyl, N(lower alkyl)C(S)lower alkyl, NHS(O)lower alkyl, N(lower alkyl)S(O)lower alkyl, C(O)OH, C(O)O-lower alkyl, $C(O)NH_2$, C(O)NH-lower alkyl, C(O)N(lower alkyl)$_2$, $S(O)_2NH_2$, $S(O)_2$NH-lower alkyl, and $S(O)_2$N(lower alkyl)$_2$.

21. The method of claim 20, wherein each R_5 substituent is independently selected from the group consisting of: alkoxy, lower-haloalkyl, S-unsubstituted alkyl, lower-haloalkoxy, unsubstituted alkyl, unsubstituted alkenyl, halogen, SH, CN, NO_2, NH_2 and OH.

22. The method of claim 21, wherein R_5 is a substituted phenyl with at least one substituent in a *meta* or *para* position selected from the group consisting of: lower alkyl, methoxy, Cl, F, Br, and lower haloalkoxy, provided that said R_5 substituted phenyl may also have 2 to 3 additional substituents.

23. The method of claim 9 or 13, wherein R_5 is an optionally substituted naphthyl.

24. The method of claim 23, wherein R_5 is a substituted naphthyl having one to four substituents each independently selected from the group consisting of: alkoxy, lower-haloalkyl, S-unsubstituted alkyl, lower-haloalkoxy, unsubstituted alkyl, unsubstituted alkenyl, halogen, SH, CN, NO_2, NH_2 and OH.

25. The method of claim 24, wherein R_5 is naphthyl.

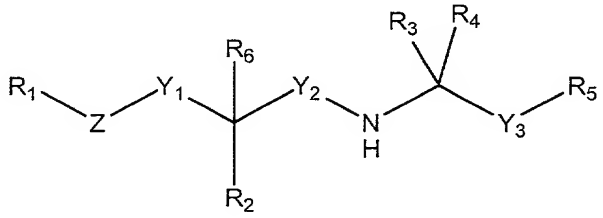
26. The method of claim 22, wherein
R_2 is OH or alkoxy,
R_6 is hydrogen,
R_3 and R_4 is each independently a lower alkyl; and
Z is either O, S, or unsubstituted alkylene.

27. The method of claim 26, wherein
R_2 is OH or methoxy;
Y_1 is methylene;
Y_2 is methylene; and
Y_3 is methylene.

28. The method of claim 27, wherein R_3 is methyl or ethyl; and R_4 is methyl or ethyl.

29. The method of claim 28, wherein Z is O or methylene and R_2 is OH.

30. A method of screening for a calcilytic compound comprising the step of measuring the ability of a compound to inhibit one or more calcium receptor activities, said compound having the formula:



wherein R_1 is selected from the group consisting of: heteroaryl and heterocycloalk;

R_2 is selected from the group consisting of: lower alk, cycloalk, alkoxy, H, OH, =O, C(O)O-lower alk, C(O)NH-lower alk, $C(O)N(\text{lower alk})_2$, SH, S-lower alk, NH_2, NH-lower alk, and $N(\text{lower alk})_2$;

R_3 and R_4 is each independently lower alk or together cyclopropyl;

R_5 is aryl;

R_6 if present is either hydrogen, lower alkyl or lower alkenyl, wherein R_6 is not present if R_2 is =O;

Y_1 is either covalent bond, alkylene, or alkenylene;

Y_2 is alkylene;

Y_3 is alkylene;

Z is selected from the group consisting of: covalent bond, O, S, NH, N-lower alk, alkylene, alkenylene, and alkynylene, provided that if Z is either O, S, NH, or N-lower alk, then Y_1 is not a covalent bond; further provided that Y_1 and Z may together be a covalent bond; and

pharmaceutically acceptable salts and complexes thereof.

31. The method of claim 30, wherein said method is carried out under conditions wherein influx of extracellular Ca^{2+} is inhibited.